STN:Search History Report

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     (FILE 'HOME' ENTERED AT 14:27:13 ON 19 JUN 2008)

     FILE 'MEDLINE, SCISEARCH, CAPLUS, BIOSIS' ENTERED AT 14:27:40 ON 19 JUN
     2008
L1             1 S CARDIAC (L) GENE THERAPY (L) CD9
L2            19 S GENE THERAPY (L) CD9
L3             8 DUP REM L2 (11 DUPLICATES REMOVED)

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L3   ANSWER 5 OF 8  CAPLUS  COPYRIGHT 2008 ACS on STN
TI   Drug for preventing or treating heart diseases comprising CD9 gene
SO   PCT Int. Appl., 45 pp.
     CODEN: PIXXD2
IN   Kosai, Kenichiro; Ushikoshi, Hiroaki
AB   A drug for preventing or treating heart diseases which comprises an
     expression vector containing CD9 gene as the active ingredient.  The
     term "heart diseases" as used above means diseases causative of heart
     failure, ischemic heart diseases, cardiomyopathy, hypertensive heart
     diseases, valvular disease, congenital heart diseases, myocarditis and
     diseases associated with arrhythmia, heart enlargement and/or frequent pulse.
     The above expression vector is a viral vector or a non-viral vector.  A
     method of preventing or treating heart diseases which comprises expressing
     the CD9 gene in the heart.  The prevention or the treatment is
     carried out by a gene therapy of transferring the
     CD9 gene.  In the gene therapy, use is made of
     a drug comprising an expression vector containing the CD9 gene as
     the active ingredient.
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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PI   WO 2005063302        A1    20050714    WO 2004-JP19774        20041224
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
     EP 1716869          A1    20061102    EP 2004-808124         20041224
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS
     US 20070161584      A1    20070712    US 2006-584109         20060622

L3   ANSWER 6 OF 8  BIOSIS  COPYRIGHT (c) 2008 The Thomson Corporation  on STN
TI   Membrane protein CD9 regulates hyperthrophy and heart failure via EGFR
     signaling in vitro and in vivo.
SO   Circulation, (OCT 26 2004) Vol. 110, No. 17, Suppl. S, pp. 8.
     Meeting Info.: 77th Scientific Meeting of the American-Heart-Association.
     New Orleans, LA, USA. November 07 -10, 2004. Amer Heart Assoc.
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CODEN: CIRCAZ. ISSN: 0009-7322.

AU Ushikoshi, Himaki [Reprint Author]; Takahashi, Tomoyuki; Esaki, Masayasu; Khai, Ngin C.; Kawai, Takao; Minatoguchi, Shinya; Fujiwara, Takako; Kosai, Ken-ichiro

AB Introduction: Cardiac hypertrophy is one of the important problems in cardiovascular diseases, because of causing heart failure. Heparin-binding EGF-like growth factor (HB-EGF) plays a large role in hypertrophic signaling and ischemia. On the other hand, protype HB-EGF forms a complex with CD9, a cell membrane protein of the tetraspanin family. Hypothesis: We hypothesized that overexpression of CD9 on heart in vitro and in vivo by adenoviral gene transduction could regulate HB-EGF function, Methods: (1) In vitro experiments: Primary cultured mouse ventricular cardiomyocytes were infected with adenoviral vector expressing CD9 (Ad-CD9). Twenty-four hours later, these cells were stimulated by angiotensin 11 (TOO nmol/1) and recombinant HB-EGF (10 ng/ml). Cell volume, beating rates and EGFR signaling were evaluated. (2) In vivo experiments: A mouse ischemic heart failure model was generated by making myocardial infarction (MI) (permanent occulusion of coronary artery). Simultaneously, Ad-CD9 , HB-EGF, CD9+HB-EGF, dE1.3 (each 1x10(11) particle, each group n=14) were directly injected into the heart. One week later, cardiac functions and histological changes were assessed. For survival rate and cardiac functions assessment, the mice were observed for eight weeks. Results: (1) Overexpression of CD9 inhibited hypertrophic effects (by angiotensin 11 and HB-EGF) on both cell volume and beating rates. Furthermore phosphorylation of mitogen-activated protein kinase and EGFR were decreased. (2) CD9 gene therapy reduced mortality in mice MI model. CD9 induction group improved cardiac function (LVEF; CD9: 46.5 +/- 3.7% VS control (dE1.3): 32.3 +/- 5.1%, p<0.05) and decreased heart weight (HW) in compared with control group (HW/Body weight; CD9: 6.52 +/- 0.31 VS dE1.3: 8.40 +/- 0.56, p<0.05). On the other hand, only HB-EGF injection group induced left ventricular hypertrophy, and high mortality within two weeks. Histological findings showed inhibition of cardiomyocyte hypertrophy (CD9: 13.3 +/- 1.88 mu m vs dE1.3: 18.1 +/- 1.55 mu m, p<0.01) at the border area, and decreasing fibrosis area (CD9: 15.5 +/- 3.7% vs dE1.3: 22.3 +/- 5.1%, p<0.05). Conclusion: CD9 gene therapy could be a potent therapy for cardiac hypertrophy and ischemic heart failure via regulation of EGFR signaling.